facsimile. Applicant's records reflect that the response was transmitted to the United States Patent and Trademark Office on March 20, 2002 at approximately 7:40 PM (EST). Accordingly, Applicant respectfully submits that the date received by the PTO should be March 20, 2002.

Applicant thanks and appreciates the Examiner for indicating that the previous rejections under 35 U.S.C. §§ 102(b) and 103(a) have been withdrawn in view of the response filed March 20, 2002.

The only outstanding rejections of the claims are under 35 U.S.C. § 102(e) (i.e., claims 1-4, 6-9, 17-20, and 22-28) over Arnon (U.S. Patent No. 5,562,907), and 35 U.S.C. §§ 102(e)/103(a) (i.e., claims 1-9 and 17-29) over Borodic (U.S. Patent No. 5,401,243. Applicant addresses those rejections herein.

II. The Office Action

Applicant is confused by some of the statements made in the Office Action. Beginning at page 3 of the Office Action, claims 1-4, 6-9, 17-20, and 22-28 have been rejected under 35 U.S.C. § 102(e). The Office Action quotes the version of 102(e) as amended by the American Inventors Protection Act of 1999 (AIPA). Then, beginning at page 5 of the Office Action, claims 1-9 and 17-29 have been rejected under 35 U.S.C. § 102(e) prior to the amendment by the AIPA. In particular, the Office Action states that "the changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre AIPA 35 U.S.C. 102(e))." (Office Action page 5).

With all due respect, and for the record, Applicant submits that the instant application was filed after November 29, 2000. **The application was filed April 30, 2001**. In addition, the instant application was voluntarily published under 35 U.S.C. 122(b). The instant application was **published on September 13, 2001 as U.S. Publication No. US 2001/0021695 A1**. Accordingly, Applicant submits that the post-AIPA version of 35 U.S.C. § 102(e) applies to the instant application. Applicant requests confirmation of this fact from the Examiner. In addition, Applicant responds herein to the rejections of the claims under 35 U.S.C. § 102(e) as § 102(e) was amended by the AIPA.

A) Items 5-6 of the Office Action - Rejections Under 35 U.S.C. § 102 by Arnon

Claims 1-4, 6-9, 17-20, and 22-28 have been rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Arnon (U.S. Patent No. 5,562,907; the '907 patent). The rejection appears to be based on the disclosure in the '907 patent of combinations of different botulinum toxins (column 13, line 60 to column 14, line 9).

Applicant respectfully traverses the rejection, and respectfully submits that Arnon (the '907 patent) is not prior art with respect to the presently claimed invention.

The '907 patent was filed on June 6, 1994 as a continuation-in-part of U.S. Application No. 08/062,110 (the '110 application), filed on May 14, 1993. As discussed herein, the disclosure in the '907 patent regarding combinations of botulinum toxins was new matter that was added to the '110 application via the continuation-in-part application, which is now the '907 patent. Accordingly, the disclosure regarding combinations of botulinum toxins in the '907 patent is **not** entitled to the May 14, 1993 priority date, and thus, the disclosure of combinations of botulinum toxins has an **effective filing date of June 6, 1994**. Because the instant application has an effective filing date of June 10, 1993, the instant application predates the disclosure of combinations of botulinum toxins of the '907 patent. Accordingly, the **'907 patent is not prior art** with respect to the claimed invention.

For the Examiner's convenience, Applicant encloses herewith a copy of the '110 application (the parent application of the '907 patent) as **Exhibit A**. Applicant submits that this copy of the '110 application is a true and correct copy of the application on record at the U.S. PTO. As the Examiner will see upon reviewing the '110 application, the '110 application does **not** disclose, or even suggest, a composition containing two or more types of botulinum toxin or methods of using such a composition. For example, the Summary of the Invention at page 15, lines 19-34 of the '110 application refer to the use of a single neurotoxin, such as botulinum toxin. In addition, page 16, lines 1-12 refer to "a toxin", "the administered toxin", "the toxin", and "the injected toxin". Furthermore, the subject matter disclosed at column 13, line 60 to column 14, line 9 is absent from the '110 application. For example, it is clear that the disclosure of combinations of botulinum toxins was added to the '110 application, by way of a CIP application, at page 18, approximately line 10, because page 18, line 8 corresponds to column 13, line 52 of the '907 patent. Thus, because the disclosure of combinations of botulinum toxins in the '907 patent is not present in the '110 application, that disclosure has an effective filing date of June 6, 1994, which is later that the effective filing date of the instant application.

Accordingly, the '907 patent is not prior art to the claimed invention, and Applicant respectfully requests the Examiner to withdraw the rejection.

B) Item 7 of the Office Action - Rejections Under 35 U.S.C. §§ 102/103 by Borodic

Claims 1-9 and 17-29 have been rejected under 35 U.S.C. § 102(e) as being anticipated by, or under § 103(a) as allegedly obvious over, Borodic (U.S. Patent No. 5,401,243).

As discussed hereinabove, Applicant is addressing the §§ 102(e)/103 rejections as amended by the AIPA. Applicant respectfully traverses the rejection that the pending

claims are anticipated by Borodic under 35 U.S.C. § 102 or obvious over Borodic under 35 U.S.C. § 103.

As stated in the Office Action (page 7), "Borodic **does not teach** specific botulinum toxin combinations (i.e. A and B, A and C, and so forth)." (emphasis added). As the Examiner is aware, a claim is anticipated by a reference only if the reference discloses each and every element recited in the claim. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.") (see MPEP § 2131). Because the Examiner has expressly acknowledged that Borodic "does not teach" botulinum toxin combinations, Borodic does not anticipate the claimed invention, and the rejection under 35 U.S.C. § 102(e) should be withdrawn.

Regarding the obviousness rejection, the Office Action states that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to include any botulinum toxin subtype or combinations thereof in the method of Borodic because Borodic et al [sic] teach that botulinum toxin-derived pharmaceuticals may take on any form of botulinum toxins A through G or various engineered proteins which retain the native form's ability to block acetylcholine release." The Office Action further states that "[i]t would have been expected, ... , that any botulinum toxin subtype or a combination thereof would be effective in treating unwanted involuntary pathologic muscle stimulations."

Applicant respectfully traverses the rejection.

First, it appears that the Examiner has mischaracterized the teachings of Borodic. The Examiner states that because Borodic teaches pharmaceuticals which may take on any form of botulinum toxin type A through G, it would be obvious to include a combination of botulinum toxins. As the Examiner is aware, a reference must be interpreted as a

whole, and cannot be picked apart to deprecate an invention (*In re Fine*, 837 F.2d 1071, 1075, (Fed. Cir. 1988)). In contrast to the Examiner's opinion, and as acknowledged by the Examiner at page 7 of the Office Action, Borodic **does not teach** combinations of botulinum toxins in pharmaceutical compositions. In contrast, Borodic repeatedly indicates that a single type of botulinum toxin is used in his compositions (for example, see column 3, line 43 ("the chemodenervating agent"); column 3, line 45 ("of toxin administered"); column 3, line 49 ("by the toxin"); column 5, line 2 ("the neurotoxin"), and column 5, line 10 ("of botulinum toxin"). Borodic never refers to the use of a composition that includes two or more types of botulinum toxin, and always refers to the botulinum toxin in the singular tense. Borodic's consistent disclosure of a single botulinum toxin actually **teaches away** from the claimed invention of compositions containing two or more types of botulinum toxin and methods of using such compositions. "As a general rule, references that teach away cannot serve to create a prima facie case of obviousness." (*McGinley v. Franklin Sports, Inc.* CAFC 8/21/01 citing *In re Gurley*, 31 USPQ2d 1131, (Fed. Cir. 1994)).

Second, the Examiner has failed to specifically indicate where in the prior art a suggestion or motivation is provided to make the claimed invention. "Although a reference need not expressly teach that the disclosure contained therein should be combined with another, the showing of combinability, in whatever form, must nevertheless be clear and particular." (*In re Dembiscak*, 175 F.3d 994, 999 (CAFC) 1999) emphasis ours). Absent such a clear and particular showing, the rejections cannot be maintained, and should be withdrawn.

Although the Examiner states that it would be expected that any botulinum toxin subtype or a combination thereof would be effective in treating muscle stimulations, the Examiner still has failed to identify a motivation or suggestion in the prior art to use compositions containing combinations of botulinum toxins. In contrast, Applicant respectfully submits that one or ordinary skill in the art prior to the time of the instant invention would not be motivated to use two or more types of botulinum toxins in a

composition. As stated by Borodic, "the pure active toxin [botulinum toxin] is believed to be the single most toxic material know[n]". (Column 1, lines 61-63). In addition, Borodic states that the outward diffusion of a toxin from its injection site is a complex and currently unknown function of, ... , the identity and amount of diluent if any injected with the toxin, the mass of the toxin, the population of presynaptic receptors about the site of injection, and the current physiological condition of the patient. (Column 6, lines 44-51). Borodic goes on to state that another factor affecting dose response is the existence of innervation zones within muscles, and that little is known about muscle innervation patterns. (Column 7, lines 14-19).

Because Borodic admits that at the time of his invention little was known about toxin diffusion and muscle innervation, clearly one of ordinary skill in the art would **not** be motivated to inject compositions containing combinations of "the single most toxic material known" into a patient given the teachings of the prior art. It was not until Applicant's reduction to practice of the presently claimed invention that compositions containing two or more types of botulinum toxin were demonstrated that they could be therapeutically effective.

In addition, Applicant respectfully submits that it was the first to realize the unexpected advantage that compositions containing two or more types of botulinum toxin permitted one to control the duration of therapeutic activity, as discussed in the instant application.

In view of the above, Applicant submits that the present claims 1 to 9 and 17 to 29 are not anticipated by and are unobvious from and patentable over Borodic under 35 U.S.C. 102(e) and 35 U.S.C. 103(a).

IV. Conclusion

Therefore, Applicant submits that the present claims, that is claims 1-9 and 17-29 are allowable. Therefore, applicant respectfully requests the Examiner to pass the above-

identified application to issuance at an early date. If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned representative invites the Examiner to telephone him at the number provided below.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on or before:

9/18/02

Andrea Uxa